

1 / 28

CTCGAGGACAGTGACCTGGGAGTGAGTACAAGGTGAGGCCACCACTCAGGGT  
GCCAGCTCCAAGCGGGTCACAGGGACGAGGGCTGCGGCCATCAGGAGGCCCT  
GCACACACATCTGGGACACGCGCCCCCGAGGGCCAGTTCACCTCAGTGCGCC  
TCATTCTCCTGCACAAAAGCGCCCCCATCCTTTCTTCACAAGGCTTTCGTGG  
AAGCAGAGGCGTCGATGCCCAGTACCCTCTCCCTTTCCCAGGCAACGGGACC  
CCAAGTTTGCTGACTGGGACCACCAAGCCACGCATGCGTCAAGAGTGAGAGT  
CCGGGACCTAGGCAGGGGCCCTGGGGTTGGGCCTGAGAGAGAAGAGAACCTC  
CCCCAGCACTCGGTGTGCATCGGTAGTGAAGGAGCCTCACCTGACCCCCGCT  
GTTGCTCAATCGACTTCCCAAGAACAGAGAGAAAAGGGAACTTCCAGGGCGG  
CCCGGGCCTCCTGGGGGTTCACACCCCATTTTCTAGCTGAAAGCACTGAGGCA  
GAGCTCCCCCTACCCAGGCTCCACTGCCCCGGCACAGAAATAACAACCACGGT  
TACTGATCATCTGGGAGCTGTCCAGGAATTC

**FIG.\_1A**

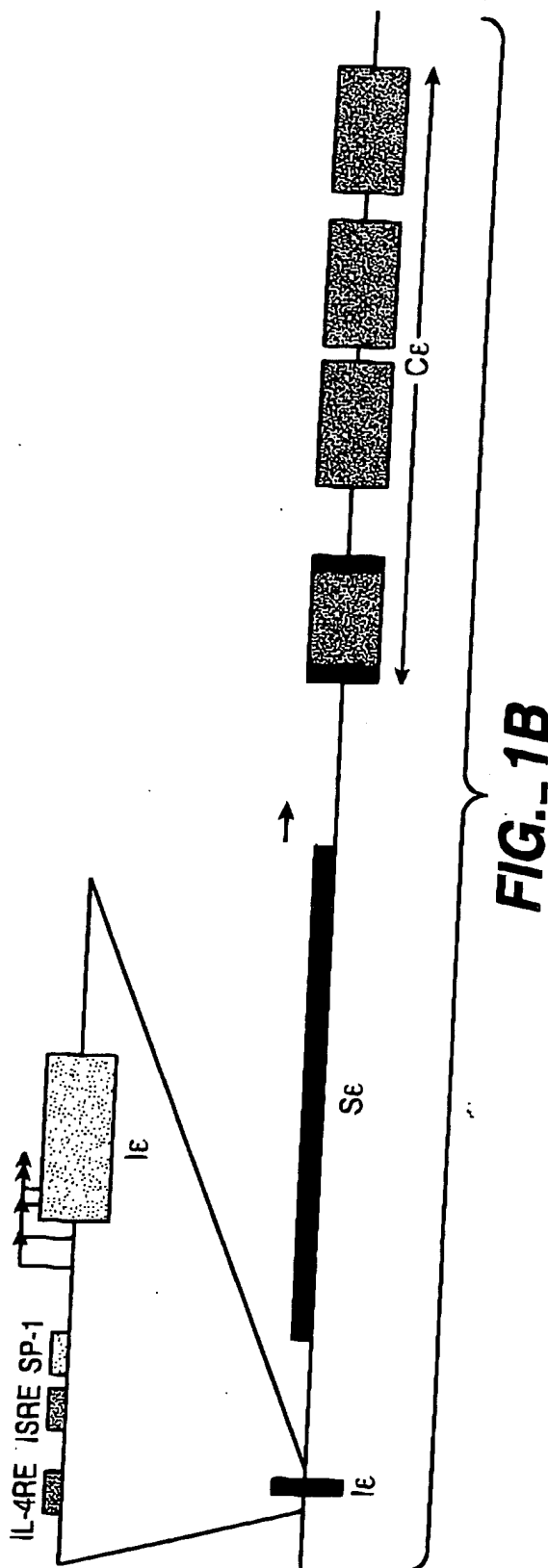
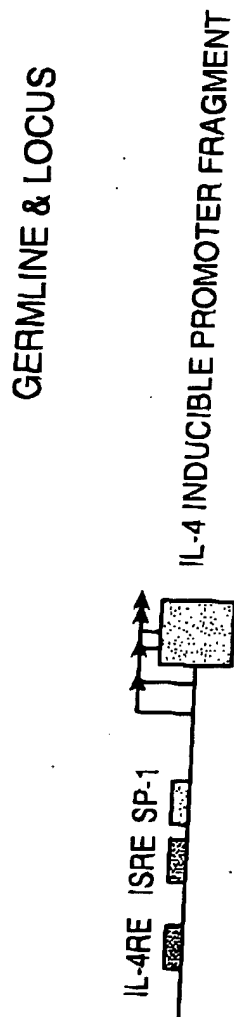
1 GCTGGGCTAA ACTGGGCTAG CCTGAGCTGG GCTGAACTGG GCTGCTGGGC  
51 TGGACTGGGT AAGCTGGGCT GAGCTGGGTT GGGTGGAAAT GGGCTGAGCT  
101 GAGCTAGGCT AAAGTGGGTT TGGCTGGGCT GGGCTGGGCT GGG

**FIG.\_2B**

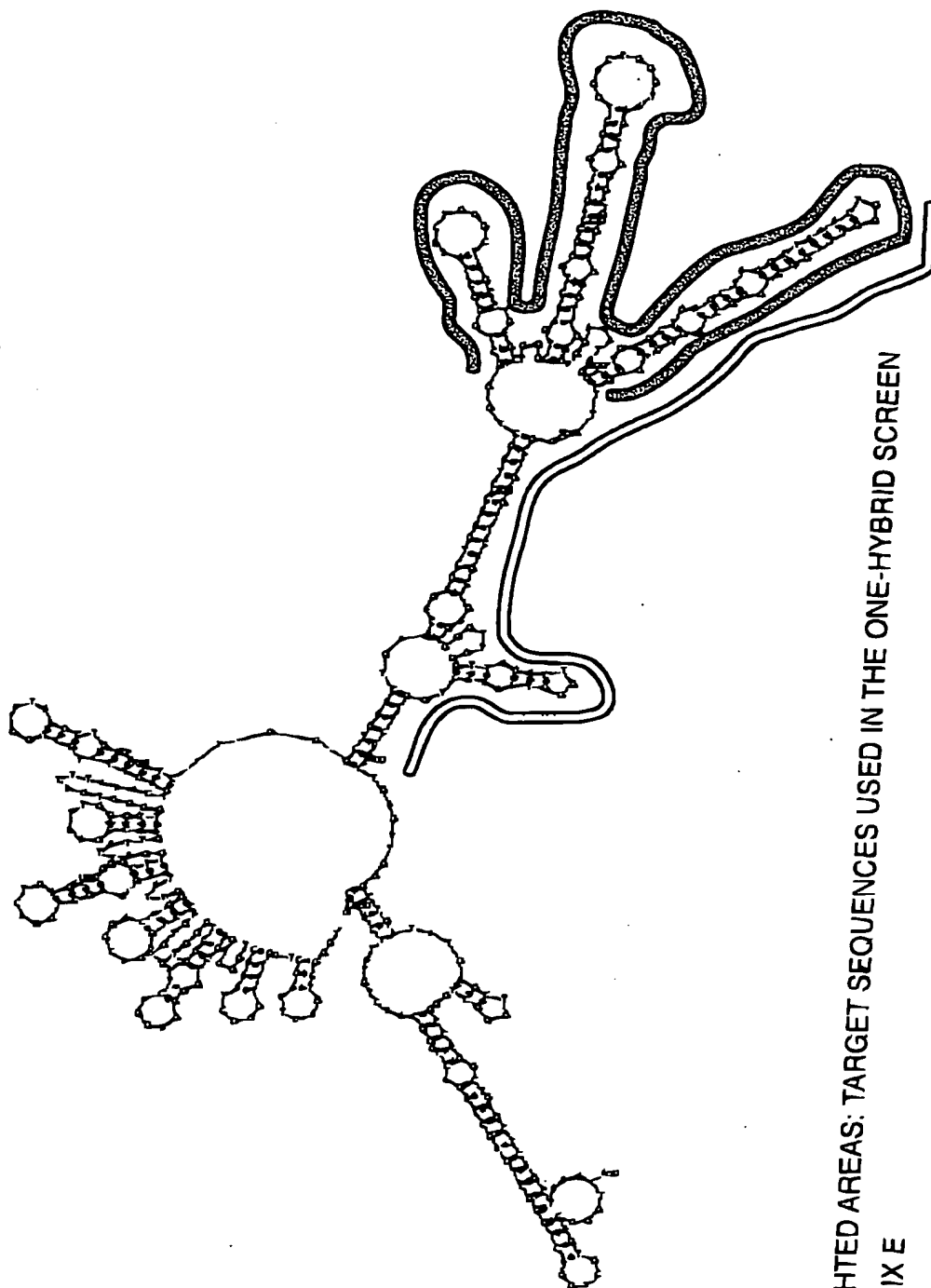
1 GGTTTGGCTG GGCTGGGCTG GGCTGGGCTG GGTTTCAGCTG AGCGGGTTGG  
51 GTTAGACTGG GTCAAACTGG TTCAGC

**FIG.\_2C**

2 / 28



# LOW ENERGY DNA FOLDING OF THE SE REGION



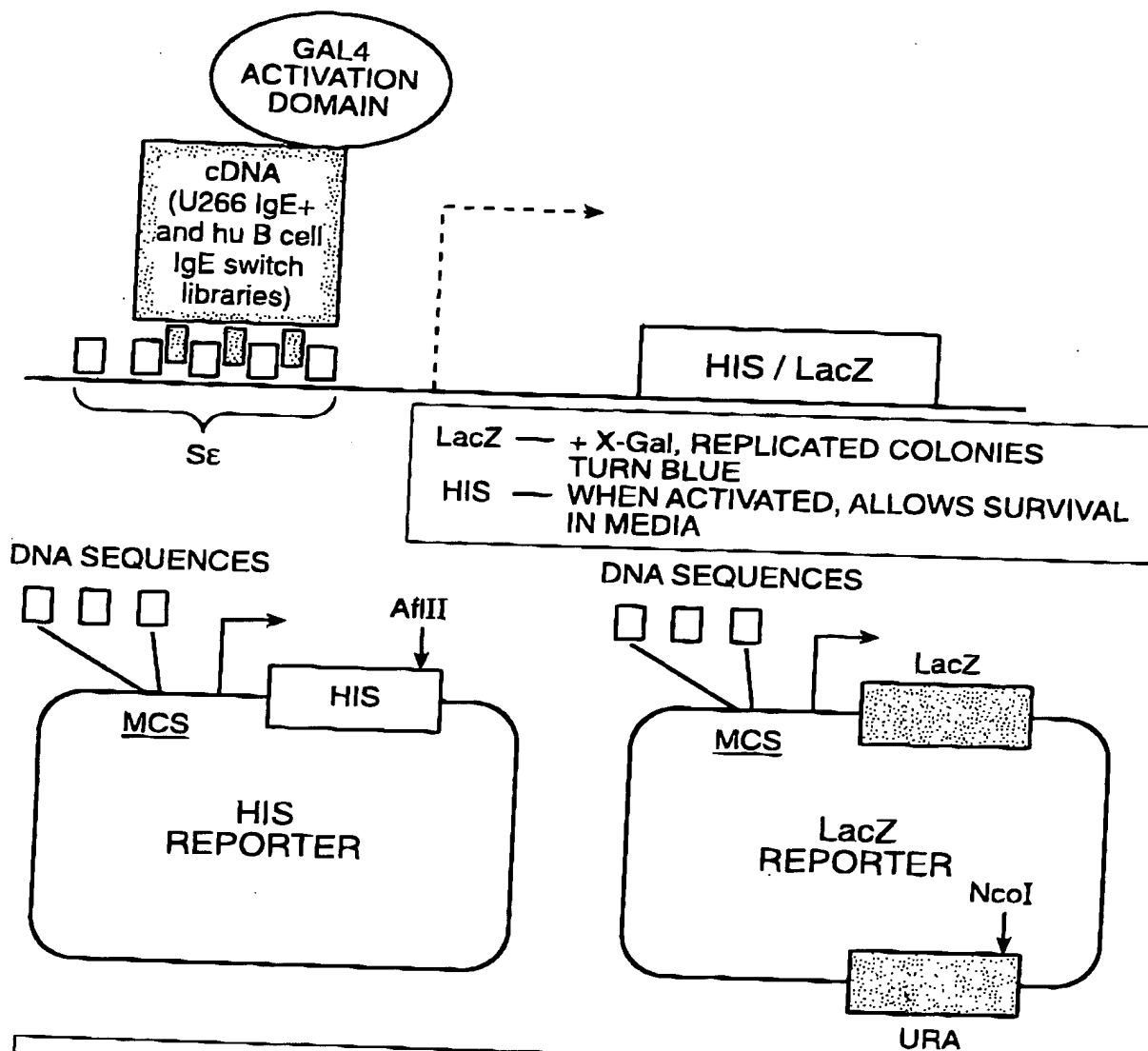
## HIGHLIGHTED AREAS: TARGET SEQUENCES USED IN THE ONE-HYBRID SCREEN

### APPENDIX E

**FIG. 2A**

4 / 28

# YEAST ONE-HYBRID SCREENING



**ONE HYBRID REPORTER VECTORS**  
 DNA SEQUENCES OF INTEREST ARE INSERTED INTO THE MULTIPLE CLONING SITES (MCS).  
 THE ENZYME USED TO LINEARIZE THE VECTOR IS SHOWN WITH A SOLID ARROW.  
 DASHED ARROWS INDICATE THE TRANSCRIPTION OF THE REPORTER GENE.

APPENDIX F

**FIG. 3**

5 / 28

IL-4 INDUCTION OF GERMLINE  $\epsilon$  mRNA IN THE  
IgM + B CELL LINES: CA-46, MC-116 AND DND39

DND39 + IL-4  
DND39 - IL-4  
MC-116 + IL-4  
MC-116 - IL-4  
CA-46 + IL-4  
CA-46 - IL-4  
NEG. CONT.



CELLS WERE INCUBATED FOR 48 HRS. IN 300 U / ml OF h-IL-4.  
RT-PCR WAS PERFORMED USING PRIMERS SPECIFIC FOR THE GERMLINE  
 $\epsilon$  EXON AND THE 5'-END OF THE C $\epsilon$  CH1 EXON (PREDICTED SIZE ~ 200 bp).  
APPENDIX G

**FIG. 4**

# APPROACHES TO GENERATE GERMLINE $\epsilon$ PROMOTER KNOCK-IN REPORTER CELL LINES

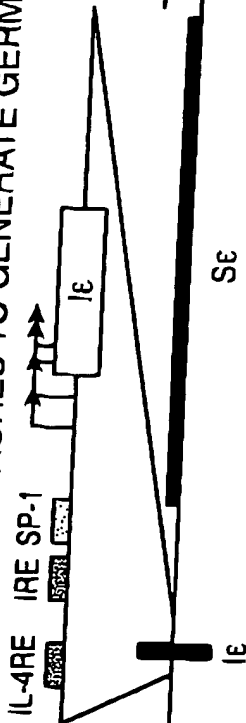


FIG. 5A

IL-4 INDUCIBLE, IgM+ B CELL LINES ARE TRANSFECTED. UNDER THE INFLUENCE OF IL-4, GFP AND / OR BFP POSITIVE CLONES ARE ISOLATED BY FACS. HOMOLOGOUS RECOMBINATION CAN BE CONFIRMED BY PCR AND/OR SOUTHERN BLOT HYBRIDIZATION.

FIG. 5B

KNOCK-IN CONSTRUCTS



IL-4 INDUCIBLE, IgM+ B CELL LINES ARE TRANSFECTED AND SELECTED WITH G418. SURVIVORS ARE SORTED FOR THE LACK OF 3' BFP EXPRESSION (DELETED DURING HOMOLOGOUS RECOMBINATION). RT-PCR IS PERFORMED TO CONFIRM HOMOLOGOUS RECOMBINATION. THOSE CLONES ARE TRANSFECTED WITH *cre* TO REMOVE THE NEOMYCIN RESISTANCE GENE.

FIG. 5C

KNOCK-IN CONSTRUCTS



6 / 28

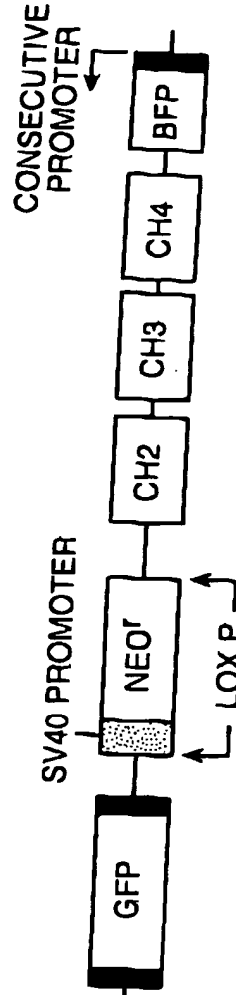
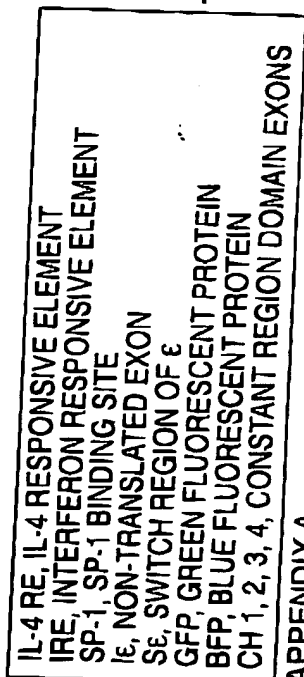
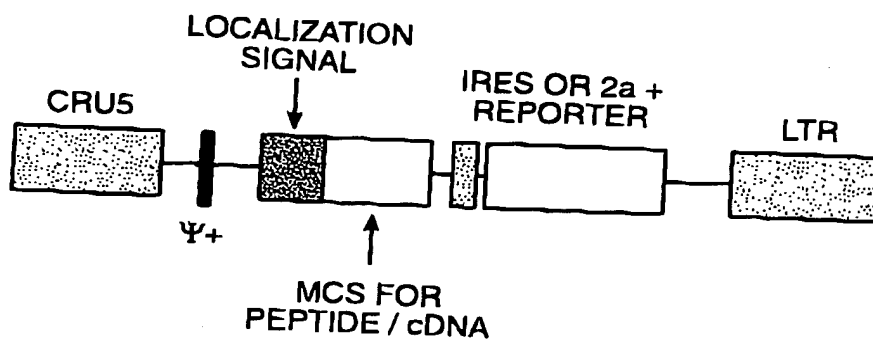


FIG. 5D

APPENDIX A

7 / 28

## RIGEL BASE VECTOR



ALL COMPONENTS ARE UNIQUELY CASSETTED FOR FLEXIBILITY

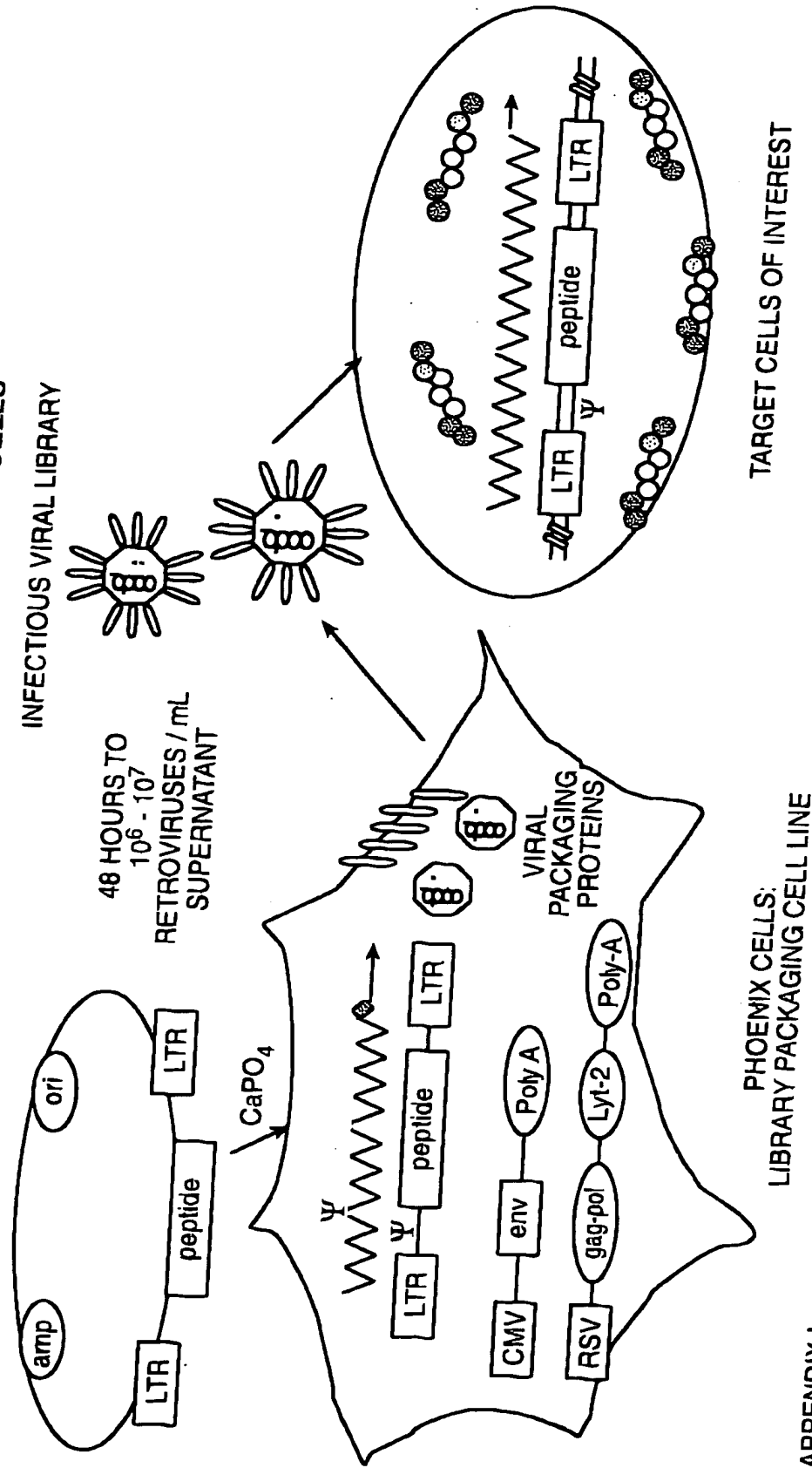
CRU5, MODIFIED LTR  
LTR, LONG TERMINAL REPEAT  
 $\Psi+$ , PACKING SIGNAL  
LOCALIZATION SIGNAL: NUCLEAR, CELL MEMBRANE, GRANULAR  
MCS, MULTIPLE CLONING SITE  
IRES, INTERNAL RIBOSOME ENTRY SITE  
2a, SELF-CLEAVING PEPTIDE

APPENDIX I

**FIG. 6**

8 / 28

# PROTOCOL FOR TRANSFECTION OF PHOENIX CELLS AND INFECTION OF NONADHERENT TARGET CELLS



APPENDIX I

FIG. 7



ε HEAVY CHAIN GFP / BFP KNOCK-IN CELL LINE  
U266 ε HEAVY CHAIN

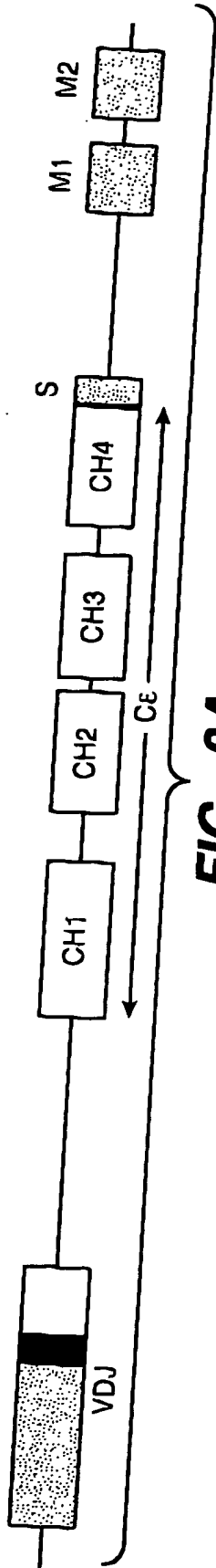
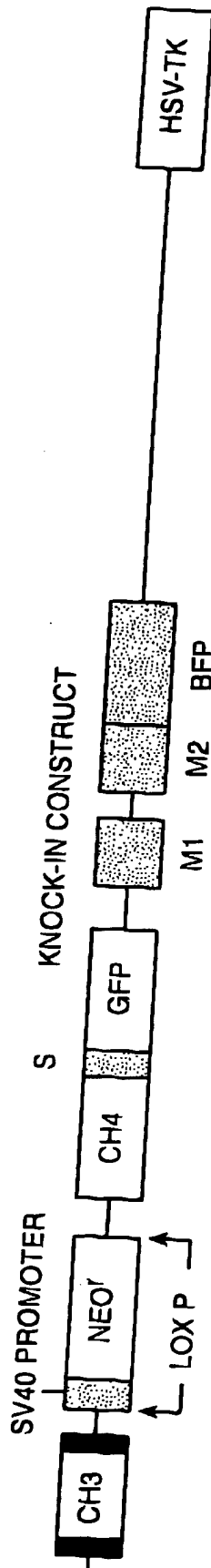


FIG. 8A

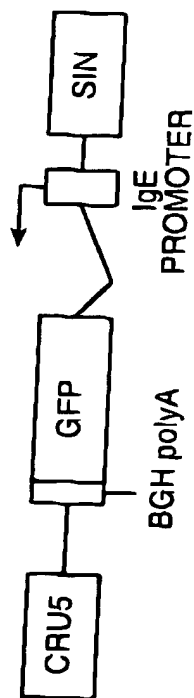


U266 CELLS ARE TRANSFECTED AND SELECTED WITH G418. SURVIVORS ARE TREATED WITH GANCICLOVIR (HSV-TK DELETED DURING HOMOLOGOUS RECOMBINATION). RT-PCR IS PERFORMED TO CONFIRM HOMOLOGOUS RECOMBINATION. THOSE CLONES ARE TRANSFECTED WITH *cre* TO REMOVE THE SV40 NEOMYCIN RESISTANCE GENE.

APPENDIX D

S, SECRETORY EXON  
GFP, GREEN FLUORESCENT PROTEIN  
BFP, BLUE FLUORESCENT PROTEIN  
Neo', NEOMYCIN RESISTANCE GENE  
VDJ, V REGION EXON  
CH 1, 2, 3, 4, CONSTANT REGION DOMAIN EXONS  
M1, M2, MEMBRANE EXONS  
HSV-TK, HERPES SIMPLEX VIRUS-THYMIDINE KINASE

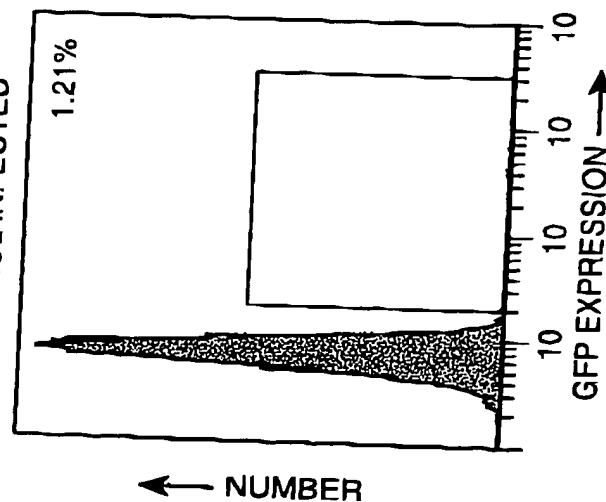
FIG. 8B

IL-4 INDUCIBLE  $\epsilon$  PROMOTER REPORTER CELL LINEREPORTER CONSTRUCT

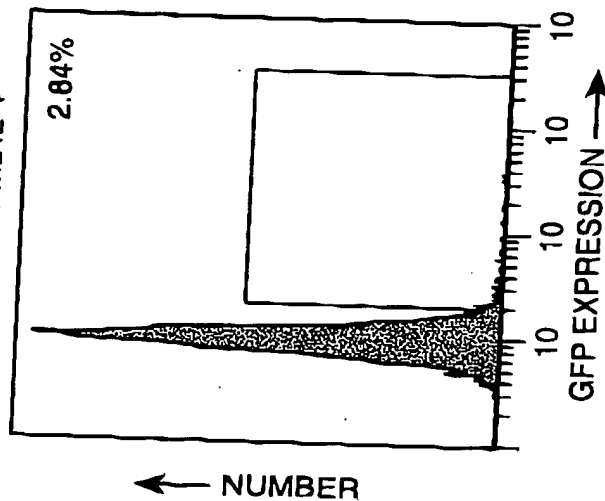
CRU5, hCMV PROMOTER PLUS R AND U5 REGIONS OF LTR  
GFP, GREEN FLUORESCENT PROTEIN  
BGH poly A, BOVINE GROWTH HORMONE poly-ADENYLATION SIGNAL  
SIN, SELF-INACTIVATING LTR

IL-4 INDUCED REPORTER

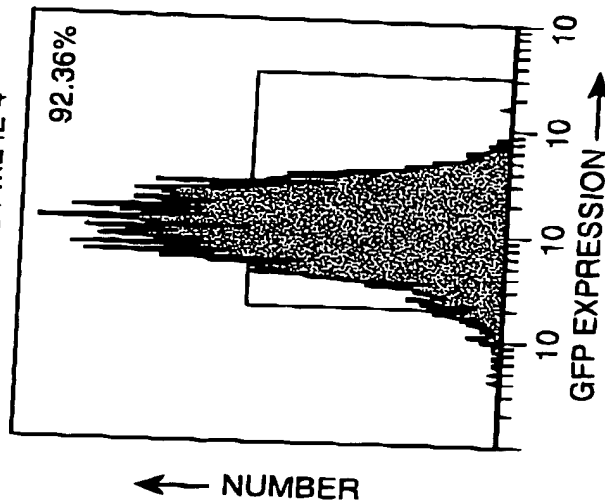
## CONTROL INFECTED



0 UNITS / mL IL-4



200 UNITS / mL IL-4

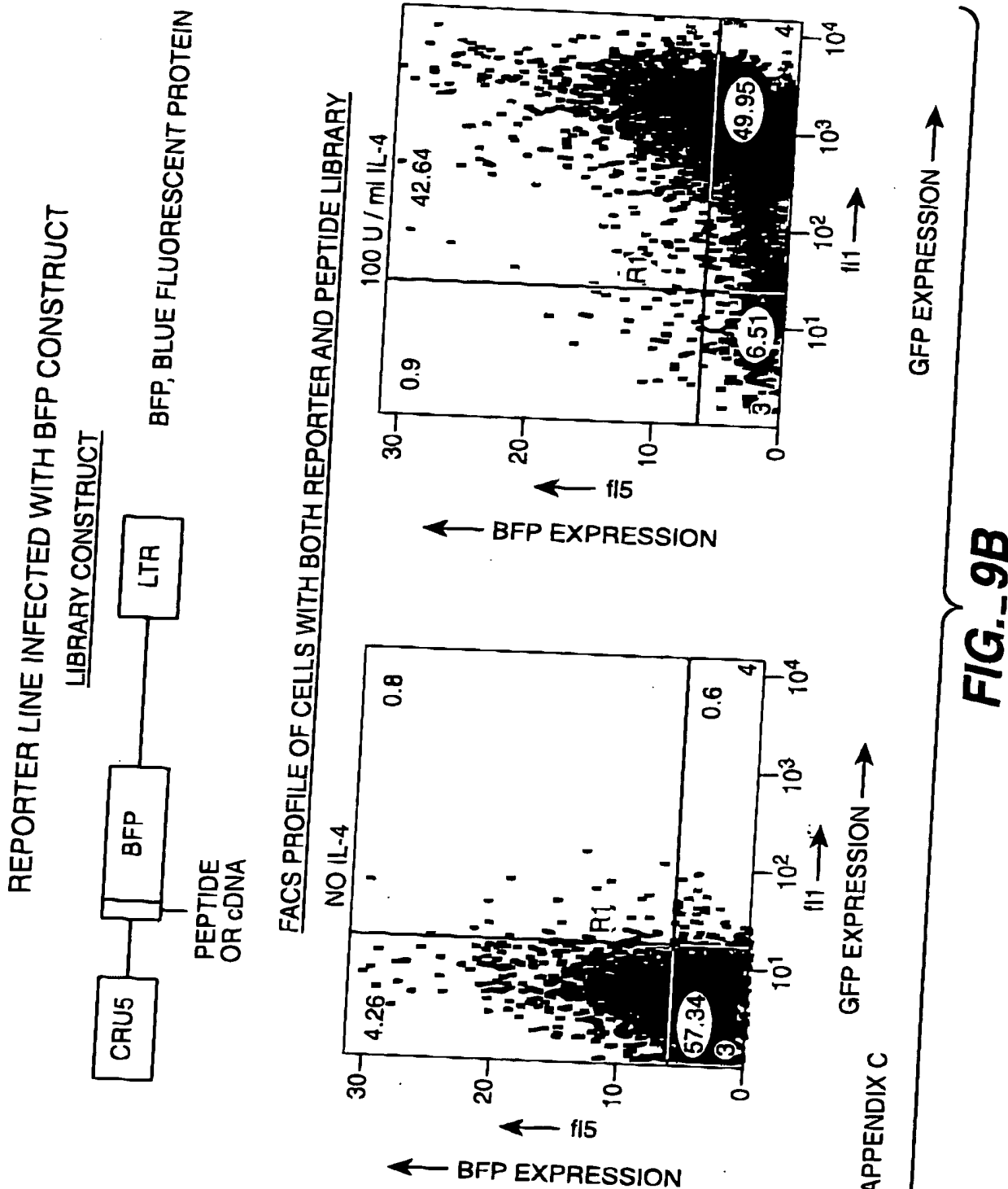


10 / 28

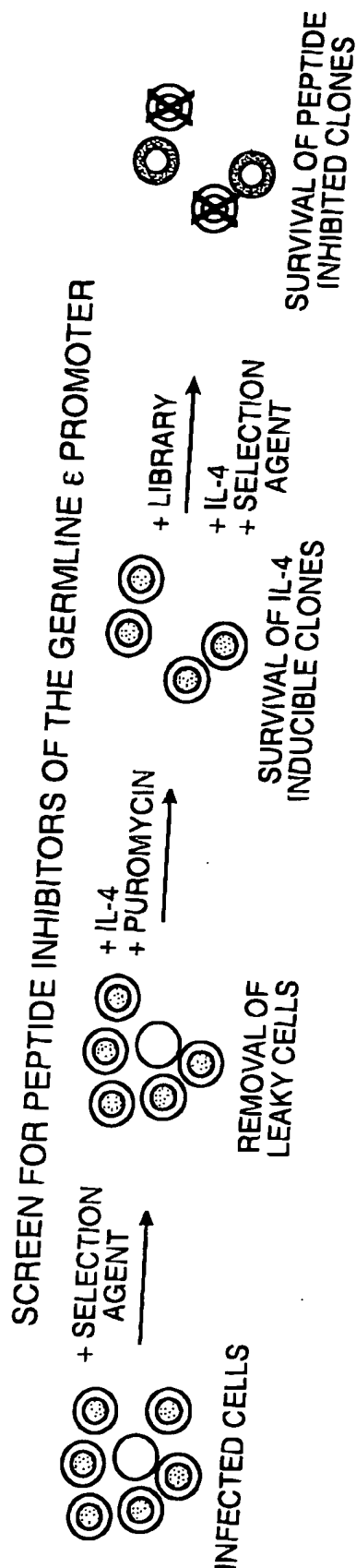
FIG. 9A

APPENDIX C

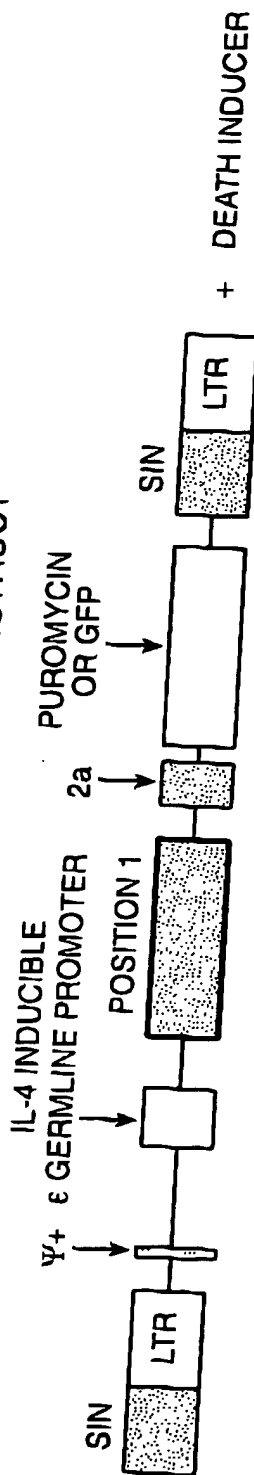
11 / 28



12 / 28



### SURVIVAL CONSTRUCT



#### POSITION 1

FAS CHIMERIC RECEPTOR\*

\*(MOUSE FASK EXTERNAL / MOUSE CD8 EXTERNAL + HUMAN TRANSMEMBRANE AND CYTOPLASMIC DOMAINS)

HSV-TK

P450-2B1

p21 PEPTIDE

SIN, SELF-INACTIVATING LTR  
LTR, LONG TERMINAL REPEAT

SELECTION AGENT  
 $\alpha$ FAS

GANCICLOVIR  
CYCLOPHOSPHAMIDE  
NONE (SELF SELECTION)

ALL COMPONENTS ARE CASSETTED FOR FLEXIBILITY

APPENDIX D

**FIG. 10**

13/28

1-845 CMV promoter/R/U5 5' LTR  
1322 GAG ATG-ATC mutation  
850-2100 extended  $\Psi$  region  
2146-2173 two Bstx1 peptide cloning sites  
2205-2723 ECMV IRES (cloned as EcoR1/MscI fragment from  
pCITE-4a [Novagen])  
2746-3465 GFP coding region  
3522-4115 3' LTR  
4122-6210 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCC  
CAAACCTCAAATATATAAAGCATTGTGACTTGTCTATGCCCTAGTTATTAATAGTAATCAA  
TTACGGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAA  
ATGGCCCCGCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATG  
TTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGT  
AAACTGCCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG  
TCAATGACGGTAAATGGCCCCGCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTT  
CTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGC  
AGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCA  
TTGACGTCAATGGGAGTTTGTGTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA  
ACAACCTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGAGGTCTATATAA  
GCAGAGCTCAATAAAAGAGCCCAACACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACT  
GAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGACGTTGCATCCGACTTGTGGT  
CTCGCTGTTCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTT  
CATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCACCGACCCACCACCG  
GGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGA  
TTTTATGCGCCTGCGTCCGGTACTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGG  
TGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAGACGTCCCAGGGACTTCGG  
GGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATCGTTTTGGACTCTTTGGTG  
CACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCC  
CGCCTCCGTCTGAATTTTTGCTTTCCGTTTGGGACCGAAGCCGCGCCGCGCTCTTGTCT  
GCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTGTTTCTGTATTTGTCTGAAAATA  
TCGGCCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATG  
TCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTACCTTCT  
GCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAG  
ACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCACTGGCCCCGCATGGACACCCAGACC  
AGGTCCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGC  
CCTTTGTACACCCTAAGCCTCCGCCTCCTCTTCTCCATCCGCCCCGTCTCTCCCCCTTG  
AACCTCCTCGTTTCGACCCCGCCTCGATCCTCCTTTATCCAGCCCTCACTCCTTCTCTAG  
GCGCCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCCGCCCCCTTGTAACCTTCC  
CTGACCCTGACATGACAAGAGTTACTAACAGCCCCCTCTCTCCAAGCTCACTTACAGGCTC  
TCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACCTGG  
ACCGACCGGTGGTACCTCACCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACC  
AGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCACCCCCA  
CCGCCCTCAAAGTAGACGGCATCGCGCTTGGATACACGCCGCCACGTGAAGGCTGCCGA  
CCCCGGGGGTGGACCATCCTCTAGACTGCCGGATCTCGAGGGATCCACCACCATGGACCC  
CCATTAAATTGGAATTCTCTGCAGCCCGGGGGATCCACTAGTTCTAGAGCGAATTAATTCC

FIG. 11A-1

14 / 28

GGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCCGGAACCTGGCCCTG  
TCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCTCTCGCCAAAGGAATGCAAGGTCTGT  
TGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAACAACGTCTGTAG  
CGACCCCTTGCAGGCAGCGGAACCCCCACCTGGCGACAGGTGCCCTCTGCGGCCAAAAGC  
CACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCAGTGCCACGTTGTGAGTTGGA  
TAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAACAAGGGGCTGAAGGATG  
CCCAGAAGGTACCCCATTTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACAT  
GTGTTTAGTCGAGGTTAAAAACGTCTAGGCCCCCCGAACCACGGGGACGTGGTTTTCTCT  
TTGAAAAACACGATGATAATATGGGGGATCCACCGGTGCGCCACCATGGTGAGCAAGGGCG  
AGGAGCTGTTTACCGGGGTGGTGCCCATCTGCTGCGAGCTGGACGGCGACGTAAACGGCC  
ACAAGTTTACGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCTGA  
AGTTCATCTGCACCACCGGCAAGCTGCCCCGTGCCCTGGCCCACCCTCGTGACCACCTGA  
CCTACGGCGTGCAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCAGCACTTCTTCA  
AGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCA  
ACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGC  
TGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAAC  
ACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAAC  
TCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGA  
ACACCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGT  
CCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCTGCTGGAGTTCTGTGA  
CCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAAAGCGGCCGCTCGACGA  
TAAAATAAAAGATTTTATTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCACCTGTA  
GGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAATAACATAACTGA  
GAATAGAGAAGTTCAGATCAAGGTGAGGAACAGATGGAACAGCTGAATATGGGCCAAACA  
GGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTG  
AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAA  
CAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTC  
CAGGGTGCCCCAAGGACCTGAAATGACCCCTGTGCCCTTATTTGAACTAACCAATCAGTTCG  
CTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCC  
TCACTCGGGGCGCCAGTCCCTCCGATTGACTGAGTCGCCCCGGGTACCCGTGTATCCAATAA  
ACCCTCTTGACGTTGCATCCGACTTGTGGTCTCGCTGTTTCTTGGGAGGGTCTCCTCTGA  
GTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCCTTGG  
GAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCACATGCAGCATGTAT  
CAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAATGGCCATAGTTGCATTAAT  
GAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTTCTCGCT  
CACTGACTCGCTGCGCTCGGTGCTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGC  
GGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGG  
CCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCG  
CCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGG  
ACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGAC  
CCTGCCGCTTACCGGATACCTGTCCGCCTTCTCCCTTCGGGAAGCGTGGCGCTTCTCTCA  
TAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTGCTTCGCTCCAAGCTGGGCTGTGT  
GCACGAACCCCCCGTTTACGCCCCGACCGCTGCGCCTTATCCGGTAACATCGTCTTGAGTC  
CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG  
AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACAC

FIG. 11A-2

15 / 28

+

TAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGT  
TGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTGTTGCAA  
GCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGG  
GTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAA  
AAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCAGCAAATCAATCTAAAG  
TATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTC  
AGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC  
GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC  
ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGG  
TCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG  
TAGTTCGCCAGTTAATAGTTTGGCGAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTC  
ACGCTCGTCGTTTGGTATGGCTTCATTTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTAC  
ATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAG  
AAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC  
TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTG  
AGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGC  
GCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACT  
CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTG  
ATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCCAAA  
TGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTT  
TCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTGGAATG  
TATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTC

FIG. 11A-3

+

16 / 28

1-845 CMVpromoter/R/U5 5' LTR  
1322 GAG ATG-ATC mutation  
850-2100 extended  $\psi$  region  
2151-2865 GFP coding region  
2866-2894 GGGSGGG linker  
2895-2952 FMDV 2a cleavage sequence  
2953-3004 Bstx1/Bstx1/HinD3/Hpa1/Sal1/Not1 polylinker  
3052-3645 3' LTR  
3652-5715 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC  
CCAAACTCAAATATATAAAGCATTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC  
AATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCGCGGTTACATAACTTACGG  
TAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCGCCCATTGACGTCAATAATGACG  
TATGTTCCCATAGTAACGCCAATAGGGACTTTCATTGACGTCAATGGGTGGAGTATTT  
ACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTA  
TTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGG  
GACTTTCCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG  
GTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTC  
TCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCA  
AAATGTCGTAACAACTCCGCCCCATTGACGCAAAATGGGCGGTAGGCATGTACGGTGGGA  
GGTCTATATAAGCAGAGCTCAATAAAAGAGCCCAACCCCTCACTCGGGGCGCCAGTC  
CTCCGATTGACTGAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGCAAGTTGCA  
TCCGACTTGTGGTCTCGCTGTTCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGT  
CAGCGGGGGTCTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCAGGGACC  
ACCGACCCACCACCGGGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTC  
TAGTGTCTATGACTGATTTTATGCGCCTGCGTCCGGTACTAGTTAGCTAACTAGCTCTGT  
ATCTGGCGGACCCGTGGTGGAAGTACGAGTTTCGGAACACCCGGCCGCAACCCTGGGAG  
ACGTCCCAGGGACTTTCGGGGGCGGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGAT  
CGTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGA  
CGAGAACCTAAACAGTTCCCGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAA  
GCCGCGCCGCGCTCTTGTCTGCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTG  
TTTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTT  
GACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAAGTCGGTAGATGTCA  
AGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGG  
CCGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTC  
ACCTGGCCCCGCATGGACACCCAGACAGGTCCCTTACATCGTGACCTGGGAAGCCTTGG  
CTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCCTAAGCCTCCGCCTCCTCTT  
CCTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTTCGACCCCGCCTCGATCCTC  
CCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTAT  
ATGGGGCACCCCCGCCCCCTTGTAAGTTCCTTGACCTGACATGACAAGAGTTACTAAC  
AGCCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAG  
ACCTCTGGCGGCAGCCTACCAAGAACAAGTGGACCGACCGGTGGTACCTCACCTTACC  
GAGTCGGCGACACAGTGTGGGTCCGCGACACCCAGACTAAGAACCTAGAACCTCGCTGG  
AAAGGACCTTACACAGTCTGTGACCAACCCCAACCGCCCTCAAAGTAGACGGCATCGC  
AGCTTGGATACACGCGCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTA  
GACTGCCGGATCTCGAGGGATCCACCATGGTGAGCAAGGGCGAGGAGCTGTTACCGGG

FIG. 11B-1



17 / 28

GTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGGCCACAAGTTCAGCGTGTC  
CGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCA  
CCGGCAAGCTGCCCCGTGCCCT GCCCACCCTCGTGACCACCCTGACCTACGGCGTGACG  
TGCTTCAGCCGCTACCCCGACCACATGAAGCAGCAGGACTTCTTCAAGTCCGCCATGCC  
CGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCC  
GCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATC  
GACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACCTACAACAGCCA  
CAACGTCTATATCATGGCCGACAAGCAGAAGAAGCGGCATCAAGGTGAAGTTCAGATCC  
GCCACAACATCGAGGACGGCAGCGTGACGCTCGCCGACCACTACCAGCAGAACACCCCC  
ATCGGCGACGGCCCCGTGCTGCTGCCCCGACAACCACTACCTGAGCACCCAGTCCGCCCT  
GAGCAAAGACCCCCAACGAGAAGCGCGATCACATGGTCTGCTGGAGTTCGTGACCGCCG  
CCGGGATCACTCTCGGCATGGACGAGCTGTACAAGGAATTCGGAGGTGGCAGCGGTGGC  
GGTCAGCTGTTGAATTTTGACCTTCTTAACTTGCGGGAGACGTCGAGTCCAACCTGG  
GCCCCACCACCACCATGGAAGCTTCCATTAAATTGGTTAACGTCGACGCGGCCGCTCGAC  
GATAAAATAAAAGATTTTATTAGTCTCCAGAAAAGGGGGGAATGAAAGACCCACCT  
GTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAA  
CTGAGAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCC  
AAACAGGATATCTGTGGTAAGCAGTTCTTCCCCGGCTCAGGGCCAAGAACAGATGGAA  
CAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCTTCCCCGGCTCAGGG  
CCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCA  
GATGTTTCCAGGGTGCCCCAAGGACCTGAAATGACCTGTGCCTTATTTGAACTAACCA  
ATCAGTTTCGCTTCTCGCTTCTGTTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGC  
CCACAACCCCTCACTCGGGGCGCCAGTCTCCGATTGACTGAGTCGCCCCGGGTACCCGT  
GTATCCAATAAACCCCTCTTGCAAGTTGCATCCGACTTGTGGTCTCGCTGTTCTTGGGAG  
GGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCGACTTGTGGT  
CTCGCTGCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCA  
CATGCAGCATGTATCAAAATTAATTTGGTTTTTTTTTCTTAAGTATTTACATTAAATGGC  
CATAGTTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCT  
CTTCCGCTTCTCCTCGCTCACTGACTCGCTCGCTCGGTCGTTCCGGCTGCGGCGAGCGGTA  
TCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAA  
GAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGG  
CGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAATCGACGCTCAAGTCAG  
AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCT  
CGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTT  
CGGGAAGCGTGCGCTTTCTCATAGCTCAGCTGTAGGTATCTCAGTTCGGTGTAGGTC  
GTTGCTCCAAGCTGGGCTGTGTGCACGAACCCCCGTTTCAGCCCCGACCGCTGCGCCTT  
ATCCGGTAACATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAG  
CAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCCTG  
AAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCT  
GAAGCCAGTTACCTTCGGA AAAAGAGTTGGTAGCTCTTGATCCGGCAAAACAAACCACCG  
CTGGTAGCGGTGGTTTTTTTTTGTGTTGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCT  
CAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAAACGAAAACCTCAG  
TTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATT  
AAAAATGAAGTTTGGCGAAATCAATCTAAAGTATATATGAGTAACTTGGTCTGACAGT  
TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCAT  
AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCC  
CCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATA

FIG. 11B-2

18 / 28

AACCAGCCAGCCGGAAGGGCCGAGCGCAGAAAGTGGTCCTGCAACTTTATCCGCCTCCAT  
CCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC  
GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTACGCTCGTCGTTTGGTATGGCT  
TCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAA  
AAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCGAGTGT  
TATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGA  
TGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCG  
ACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAACTT  
TAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACCTCTCAAGGATCTTACCG  
CTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTT  
TACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAGG  
GAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGA  
AGCATTTATCAGGGTTATTGTCTCATGACATTAACCTATAAAAATAGGCGT

**FIG.\_11B-3**

19/28

1-845 CMV promoter/R/U5 5' LTR  
1322 GAG ATG-ATC mutation  
850-2100 extended  $\psi$  region  
2146-2173 two Bstx1 peptide cloning sites  
2173-2214 EcoRI/ApaI/HpaI/NotI polylinker  
2262-2855 3' LTR  
2855-4901 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC  
CCAAACTCAAATATATAAAGCATTGTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC  
AATTACGGGGTCATTAGTTCATAGCCATATATGGAGTTCCGCGTTACATAACTTACGGT  
AAATGGCCCGCCTGGCTGACCGCCCAACGACCCCGCCCATTTGACGTCAATAATGACGT  
ATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTA  
CGGTAAACTGCCCACCTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTAT  
TGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG  
ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGG  
TTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGAATCACGGGGATTTCGAAGTCT  
CCACCCCATTTGACGTCAATGGGAGTTTGTGTTTGGCACCAAAATCAACGGGACTTTCCAA  
AATGTCGTAACTCCGCCCCATTGACGCAAAATGGGCGGTAGGCATGTACGGTGGGAG  
GTCTATATAAGCAGAGCTCAATAAAGAGCCCAACCCCTCACTCGGGGCGCCAGTCC  
TCCGATTGACTGAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGACGTTGCAT  
CCGACTTGTGGTCTCGCTGTTCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTC  
AGCGGGGGTCTTTCATTGTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCA  
CCGACCCACCACCGGGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCT  
AGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAAGTCTGTCTGTA  
TCTGGCGGACCCGTGGTGGAACTGACGAGTTTCGGAACACCCGGCCGCAACCCTGGGAGA  
CGTCCCAGGGACTTCGGGGGCGGTTTGTGGCCCCGACCTGAGTCCAAAAATCCCGATC  
GTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGAC  
GAGAACCTAAAACAGTTCCCGCCTCCGTCTGAATTTTGGCTTTTCGGTTTGGGACCGAAG  
CCGCGCCGCGCGTCTTGTCTGCTGACGATCGTTCTGTGTTGTCTCTGTCTGACTGTGT  
TTCTGTATTTGTCTGAAAAATATCGGCCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTG  
ACCTTAGGTCACTGGAAAGATGTGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAA  
GAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAAATGGCCAACCTTTAACGTCCGATGGC  
CGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTAAAGATCAAGGTCTTTTCA  
CCTGGCCCCGCATGGACACCCAGACAGGTCCCCCTACATCGTGACCTGGGAAGCCTTGGC  
TTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCTCCTCTTC  
CTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTTCGACCCCGCCTCGATCCTCC  
CTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATA  
TGGGGCACCCCCGCCCCCTTGTAACCTTCCCTGACCCCTGACATGACAAGAGTTACTAACA  
GCCCCCTCTCTCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAGA  
CCTCTGGCGGACAGCTGTGGGTCCGCGGACACCAGACTAAGAACCCTAGAACCCTCGCTGGA  
AAGGACCTTACACAGTCCTGCTGACCACCCCAACCGCCCTCAAAGTAGACGGCATCGCA  
GCTTGGATACACGCCGCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTAG  
ACTGCCGGATCTCGAGGGATCCACCACCATGGACCCCCATTAAATTGGAATTCGGGGCC  
CAAGCTTTGTAAACGTGACGCGGCGCGGTCGACGATAAAATAAAGATTTTATTTAG  
TCTCCAGAAAAAGGGGGGAATGAAAGACCCACCTGTAGGTTTGGCAAGCTAGCTTAAG  
TAACGCCATTTTGAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCA

FIG. 11C-1

20 / 28

AGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAG  
TTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTGAATATGGGCCAAACAGGA  
TATCTGTGGTAAGCAGTTCTTCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATG  
CGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGA  
CCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTTCGCTTCTCGCTTCTGTT  
CGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCC  
AGTCCTCCGATTGACTGAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGACAGT  
TGCATCCGACTTGTGGTCTCGCTGTTCTTGGGAGGGTCTCCTCTGAGTGATTGACTAC  
CCGTCAGCGGGGGTCTTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGGGAGGGTCTCCT  
CTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTCACATGCAGCATGTATCAAAATTAAT  
TTGGTTTTTTTTTCTTAAGTATTTACATTAAATGGCCATAGTTGCATTAATGAATCGGCC  
AACGCGCGGGGAGAGGGCGGTTTTCGTATTGGCGCTCTTCCGCTTCTCCTCGCTCACTGACT  
CGCTGCGCTCGGTGCTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATA  
CGGTTATCCACAGAATCAGGGGATAACGCGAGGAAAGAACATGTGAGCAAAGGCCAGCA  
AAAGGCCAGGAACCGTAAAAAGGCCGCGTGTGGCGTTTTTCCATAGGCTCCGCCCCC  
CTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTA  
TAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCT  
GCCGCTTACCGGATACCTGTCCGCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATA  
GCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTGCTTCGCTCCAAGCTGGGCTGTGTG  
CACGAACCCCCCGTTACGCCCCGACCGCTGCGCCTTATCCGGTAAGTATCGTCTTGAGTC  
CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCA  
GAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC  
ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAG  
AGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTTGTTT  
GCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCT  
ACGGGGTCTGACGCTCAGTGGAACGAAACTCACGTTAAGGGATTTTGGTTCATGAGATT  
ATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAATAATGAAGTTTGGCGCAAATCAA  
TCTAAAGTATATATGAGTAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCA  
CCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCCGTCGTGTA  
GATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAG  
ACCCACGCTCACC GGCTCCAGATTTATCAGCAATAAACAGCCAGCCGGAAGGGCCGAG  
CGCAGAAGTGGTCTGCAACTTTATCCGCTCCATCCAGTCTATTAATTGTTGCCGGGA  
AGCTAGAGTAAGTAGTTTCGCCAGTTAATAGTTTGGCGAACGTTGTTGTCATTGCTACAG  
GCATCGTGGTGTACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGA  
TCAAGGCGAGTTACATGATCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCC  
TCCGATCGTTGTGTCAGAAGTAAGTTGGCCGCGAGTGTTATCACTCATGGTTATGGCAGCAC  
TGCATAATTCTCTTACTGTCTATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC  
TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTC  
AACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAGTGCTCATCATTGGAAAAC  
GTTCTTCGGGGCGAAAACCTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTTCGATGTAA  
CCCCTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTTACCAGCGTTTCTGGGTG  
AGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGGAATAAGGGCGACACGGAAATGTT  
GAATACTCATACTCTTCTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTC  
ATGACATTAACCTATAAAAATAGGCGT

FIG. 11C-2

21 / 28

## (1) C12ScFas Survival construct

C12ScFas: epsilon-cFas(CD95)-Ires-Hygro-BGH polyA put into C12s vector backwards so that no leaky transcription happens through the cmv promoter.

atcacgaggcccttctgtcttcaagaacagccttctgtctcttaggaggttctcctaataacatccccaaactcaaatatataaagc  
atttgacttgttctatgccctagttatttaataagtaataacattacgggtcatttagttcatagcccatatataaagc  
cgttacataaacttacggttaaatggccgcctggtgacgcccacgaccccccgccttgaagcgtcaaatgaggttccg  
ttcccatagtaacgccaatagggaactttccattgacgtcaatgggtggagatttacggtaaaactgccacttggcagta  
catcaagtgatcatatgccaagtacgcccctattgacgtcaatgacggttaaaatggccgcctggcattatgcccagta  
catgaccttatgggactttccctacttggcagtaacatcactgatttagtcacgtctatgacgtcaatgggagtttg  
agtacatcaaatgggctggatagcgggttggactcaggggatttccaaagtctccacccattgacgtcaatgggagtttg  
ttttggcaccacaaatacaacgggactttccaaagtctcgttaacaaactcgcacccattgacgtcaatgggagtttg  
acggtgggaggtctatatagaacagagctcaataaaagagcccaacccctcactcggggcgcagtcctccgattgact  
gagtcgcccgggtaccctgtatccaataaaacctcttgcagttgcactcgggtgtgtgtctgtctgttcttcttgggaggg  
tctcctctgagtgattgactaccctgacgggggtcttcttattgggggctcgtccgggacgtggtctgtctgtctgtctgt  
ggacacccgacccacccacgggaggttaagctggccagcaacttatttgggggctcgtccgggacgtggtctgtctgtctgt  
tcttatggcctcgtcgtggtactagttagctaaactagctctgtatctggtgggacccctggtggaaactgacgagttcggaa  
caccggcgcgaacctgggagacgtccacgggacttccggggccttcttggggcgcctggtggaaactgacgagttcggaa  
tcggtttggactcttgggtgcaccccttagaggagggatattgtgtcttgggtcctggttaggagacgagaaactccgaa  
cgctccgctcgtgaattttgtcttctgtatttgggttgggacggaagcgcgcgcgtcttctgtctgtcgtcagcactcgttctgtgt  
tcttaggtcactggaaagatgtcgagcggatcgtctcaacacacagtcggtagatgtcaagaagagacgttgggttacctt  
gctctgcagaatggccaaaccttaacgtcggatggccgagacgggacaccttaacggagacacctcaacccaggttaag  
atcaagggtctttcacctggccgcatggacacccagacaggtccctacatcgtgacctgggaagccttgggttaccttct  
ccccctcctgggtcaagcccttggtaacacctaaagcctccgctccttctcctccatccgcccgtctctcccccttg  
aacctcctcgttcgaccccgctcgatcctccttataccagccctcaactccttctctagggcgcacccatagggccat  
gagatcttatatggggcaccccccgttggtaaaactcctgacccctgacatgacaagagttactaaacagccccctctct  
ccaagctcacttacagggtctctacttagtcacgacgaagtctggagacctctggcgcagcctaccacgaacacactct  
accgacccggtggtaacctcaccttaccgagtcggcgacacagtggtgggtccgcgacacccagactaaagaacctaggg  
cgctggaaaggacaccttacacagtcctgtagcaccacccacccctcaaaagttagcgggcatcgagcttggatcacacgc  
cgccacgctgaaggctgcgaccccggggtggaccatcctcttagactgcccggatctcgagggatctccccCAGCATGCC

TGCTATTGTCTTCCCAATCTCCCCCTTGCTGTCTTGCCCCACCCCCACCCAGAAATAGATGACACCTACTCAGACAA

TGGGATGCAATTCTCTCATTTATTAGGAAAGGACAGTGGGAGTGCCACCTTCCAGGGTCAAGGAAGGCACGGGGAGGG

GCAACAACAGATGGCTGGCAACTAGAAAGGCACAGTCGAGGCTAGCTTGCCAAACCTACAGSTGGGGTCTTTTCATTCCC

FIG.-12A

22 / 28

FIG.- 12B

CCCTTTTCTGGAGACTAAATAAAATCTTTTATTTATcgcataagatcccggctcggcatctactctatctccttgcctcgcg  
gcgagtgcctggggcgctcggtttccactatcggcgagtagtctctacacagccatcgggtccagacgcccggcctctcgcgg  
gcgatttgtagcgcgcgacagtcgccgctccggatcggacgattcgctgcgcatcgaccctcgcccaagctgcacatc  
gaaatgcgcgtcaaccaagctctgataagattggtcaagaccaaagcgaggacataacgcccggagccgcccgcgacatcctg  
caagctccggatgcctccgctcgaagtagcgcgtctgctcctacatacaagcccaaccacgcccctccagaaagagatggtg  
gcgacctgtaattgggaatcccgcgaacatcgctcgcctccagtcgaatgaccgctggttatcgggccatgtccgtcaggac  
attggtggagccgaaatccgcgtycacgaggtgcgggacttcgggacgtccctcgcccacagcatcagctcatcgagag  
cctgcgcgacggagcactgacggtgctgctccatcacagtttgccagtgatacacatgggacagcaatcgggcataatg  
aaatcacgccaatgtagtattgacccgattccttgcggtccgaatggccgaacagggcgagttcggtttcaggcaggtcttgcaacgtgacac  
agcatcgcatccatggcctccgcgacccgctgcgaacacgagggcgagttcggtttcgggttcgaagcacttcgggaatcgggagcgcg  
cctgtgcaacggcgagatgcaataggctcaggctctcgctaaattcccacatgtcaagcacttcgggaatcgggagcgcg  
gccgatgcaaaagtgcgataaacataaacgactcttgtagaaacacatcggcgagctgcatcaggtcggagacgctgtcgaacttt  
ccctcctacatcgaagctgaagcacgagatctcttgccctccgagagctgcatcaggtcggagacgctgtcgaacttt  
cgaatcagaaactctcgacagacgctcggtgagttcaggcttttcaatggtattatcatcgtgtttttcaaaaggaaac  
atcagatcccatacaatgggttaccttctgggcatccttcagcccttgactaaacacatgtaagcagctgtgacccgagggcccg  
tttccacaactatccaaactcaaaagtggaactgggttggtgcgccttggaatcgccttgaggagagccatttgactc  
ccgcagggcacctgtcgccaggtgggggttcgctgcctgcaaaaggctcgctacagagctgtgttctcctcaagaaagc  
ttCCAGAGGAAC TGCTTCCTTCACGACATTCAACAGACCTTGCAATTCCTTTGGCGAGAGGGGAAAGACCCctagactaga  
ccaagcttggatttcatttctgaagtttgaatttctgagtcactagtaattgctccttgaggatgatatgtcgaattttc  
ctgcaagagtacaaagattggcttttttgagatcttcaatcaatgtgtcatcagcttcttcttccatgaagttagt  
cgaaccattcttccgaacaaagcctttaaacttgacttagtgctcagcactcagctccagcaaatggtggtgatatatttggcttcat  
tcaacatcagataaaatttatggcactgtttcaggatttaagggtggagattcattggaacccctgggttttcccttctctg  
cttctgcatgtttctgtacttcccttcttccacccaaacaaatagtggaatttggcaaaagaaagaaagaaagccacc  
ccaacccggttTCTGGGACTTTGTTTCCTGCGAGTTTGTATTTGCTGGTTGCTGTGCATGGCTCAAGGGTTCCATGTTTCACAC  
GAGGCGCAGCGAACAACAGTGTTTCACAGCCAGGAGAAATCGCAGTAGAAGTCTGGTTTGCACCTTGCACTTGGTATTCTGGGT  
CAGGGTGCGAGTTTGTTTCCACTTCTAAACCAATGCTCTTTCATCGCAGAGTGTTGCATCTTCTGCACTTATATCAGCATAAATGGT  
TCTTGTCCATGTACTCCTTCCCTTCTGTGCATGGGGCACAGGTTGGTGTACCCCCATTCAATTTTGCAGTCTCCTCAACTTTT  
TTTTTACCAGGTTGGCATGGTTGACAGCAAAATGGGCCCTCCTTGATATAATCCTTCTGAGCAGTTTTATCAGTTTTCATG  
AACCCGCCCTCCTCAGCTTTAAACTCTCGGAGATGCTATTAGTACCTTGAGTATGAACCTCTTAACCTGTGAGCCAGCAAGCA

23 / 28

FIG.-12C

CCAGAGGCAGGACAGCCAGATCCACACCATGTTGGCTTTACCAACAGTACCGGAATGCCAAGCTTGCGGCCGCTTAAAGA  
GCTGTAATTGAACCTGGGAGTGGACACCTGTGGAGAGAAAGGCAAAAGTGGATGTCAATAAGACCAATAGGTGCCCTATACAG  
AAACGCAAGAGTCTTCTCTGTCTCGACAAGCCAGTTTCTATTGGTCTCTCTTAAACCTGTCTTGTAACTTGTACTTACTTAC  
CTGCCCAGTGCCTCACGACCAACTTctgcaggaaattcctggacagctccccagatgatcagtaaccgtggttgttatttct  
gtgcggggcagtggaacctgggtaggggagctctgcctcagtgctttcagctaaaaatggggtgggaaccccoCaggaag  
ctcaactaccgatgcacacccagtgctggggagggttctctctctgggaagtcgattgagcaacagcgggggtcaggtgaggtctcc  
ggaactctCactcttgcagcatgctggcttgggtccccagtcagcaaaacttggggtcccgctgcctggaaaggagag  
ggtaactgggcatcgacgacctctgcttccacgaaggccttgtgaagaaaggatgggggcgcttctgtgcaggaagaaatgag  
cgcaactgaggtgaactggccctcggggGcgctgtccccagatgtgtgagggccctcctgatggccgcagccctcgtcc  
ctgtgacccgcttggagctggcaacctgagtggtggcctcacCTTGTACTCACTCCAGGTCACTGTCTCTcgaCGCGGCC  
GCTCGAcgatAAAAATAAAGATTTTATTAGTCTCCAGAAAAGGGGGAATGAAGACCCACCTGTAGGTTTGGCAAG  
ctagCTTAAGTAACCCATTTTGCAAGGCATGGMAAAATACATAACTGAGAATAGAGAAGTTCAGATCAAGGTCGGAACAG  
ATGGAACAGGCCAATAAAGAGCCCAACCCCTCACTCGGGGCGCCAGTCTCCGATTGACTGAGTCGCCCGGGTACCCG  
TGATATCCAATAAAACCTCTTGCAAGTTGCATCCGACTTGTGGTCTCGCTGTTCTTGGGAGGGTCTCCTCTGAGTGATTGA  
CTACCCGTCAGCGGGGCTCTTTCacatgcagCATGTATCAAAATTAATTTGGTTTCTTTCTTAAGTATTTACATTTAAAT  
GGCCATagtttcGTAATCATGGTCATAGCTGTTTCTGTGTGAATTTGTTATCCGCTCACAAATTCACACAACATACGAG  
CCGGAAGCATAAAGTGTAAGCCTGGGGTGCCTAATGAGTGAGCTNACTCACATTAATTGCGTTGCGCTCACTGCCCGCT  
TTCCAGTCGGGAAACCTGTCTGCGCAGCTGCATTAATGAATCGGCCAACCGCGGGGAGAGCGGTTTGCGTATTGGCGG  
CTCTTCCGCTTCCCTCGCTCACTGACTCGCTGCTCGGCTCGGCTCGGCGGAGCGGTATCAGCTCACTCAAAAGGCGG  
TAATACGGTTATCCACAGAAATCAGGGGATAACGCAGGAAGAAACAATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGT  
AAAAAGGCCCGCTGCTGGCGTTTTCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAG  
GTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAAGCTCCCTCGTGGCGCTCTCTGTTCGACCC





25 / 28

(2) Abhhh: Survival construct

2.) Abhhh: epsilon-cFas' (CD8 or mUyt2) -Ires-Rygro-BGHPolyA also in C12s backwards

atcacgaggcccttctcgctcttcaagaacagcttctgctcttaggagttctcctaatacatcccaaaactcaaatatataaaagc  
attgactgttctatgcccctagttattaatagtaaatcaattacggggtcattagttcatagcccatatattggagttcccg  
cgttacataaacttacggttaaatggcccgctggctgacgcccacgacccccgcccatggacgtcaataatgacgtatg  
tcccataagtaacgcaatagggaacttccattgacgtcaatgggtggagattttacggtaaactgcccaacttggcagta  
catcaagtgtatcatatgccaaagtacgccccctattgacgtcaatgacggttaaatggcccgctggcattatgcccagta  
catgacctatgggaacttctacttggtgagtgatagcgttctgactcaagggtattcgaagtctccacccattgacgtcaatgggagtttg  
agtaacatcaatggcggtggtggtttagctcaagggtattcgaagtctccacccattgacgtcaatgggagtttg  
tttggcaccaaaatcaacgggaacttccaaaatgtcgttaacaaactccgccccattgacgtcaatgggagtttg  
acggtggaggtctatatagaagcagagctcaataaaagagcccaaacccctcactcggggagcagtcctcgatggatgt  
gagtgcggcggtacccgtgtatccaaataaaacccctcttgacgttgcatccgacttgggtctcgctgttcttgggaggg  
tctcctctgagtattgactacccgtcagcggggtcttcttcaattgggggtcgtcgtcggtcttcttgggaggg  
ggacacccgacccacccggtggttaagctggccagcaacttattgtgtctgtccgaattgtctagtgactgactga  
ttttatgcgctcggtcggtactagtttagctaaactagctctgtatctggggacccgtgggtggaactgacgagttcggaa  
cacccggcggcaacccctgggagagctcccgaggacttccggggcggttttggggccgacctgagtcgaacaaatcccgga  
tcggtttgggactcttgggtgcaaccccttagaggaggggatatgtggttctggttaggagacgagaacctaacaacgttcc  
cgcctcgtctgaatttctgtatttctgtatttctgaaataatgggcccggcgccggtcttctgtctgctgagcagtcgttctgtgt  
cttaggtcaactggaagatgtcgagcggtatcgctcacaaccagtcggtagatgtcaagaagagagcgttgggttaccttct  
gctctgcagaatggcccaacctttaacgtcggatggccgagacgggacactttaaccgagacactcatcacccaggttaag  
atcaagggtctttcacctggcccgcatggacacccagacccaggttccctacatcgtgacctgggaagccttgggttttga  
ccccctcctgggtcaagcctttgtacacccctaagcctccgctcctcttcttccatccgccccgtctctcccccttg  
aactcctcgttcgacccccctcgatcctccttcttccagccctcactccttcttctagggcccccatatggccat  
gagatcttatatggggcacccccctgttaacttccctgacctgacatgacaagagttactaacagccccctctct  
ccaaagctcaactacagggtctctacttagtccagcacgaagctctggagacctctggcgagccttaccaagaacaaactct  
accgacgggtggtaacctacaccttacagagtcggcgacacagtggtgggtccgcccagacaccagactaaagaacctaagcct  
cgctggaaagggaaccttacacagtcctgctgacacccccacccgacctcaagtagacgggcatcgagcttggatacacgc  
cgccccagctgaaggctgccgacccccgggggtggaccatcctctagactgcccggatcttcgagggtcctccccagcatgccc  
TGCTATTGTCTTCCCAATCCTCCCCCTTGCTGTCTGCTGCCCCACCCACCCAGAAATAGAAATGACACCTACTCAGACAA

TGCGATGCAATTTCCCTCATTTTATTAGGAAGGACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGAGGGG

GCAAAACACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGCTTAGCTTGCCAAACCTACAGGTGGGTCTTTTCATTCCC

FIG.-13A

26 / 28

CCCTTTTCTGGAGACTAAATAAAATCTTTTATTTTatcgatagatcccggctggcatctactcttgcctctg  
gacgagtgctggggctgggttccactatcggcgagtagtcttccacagccatcggtccagacggccgctctgcctc  
gcgatttctgtacgcccagactcccggtccggatcggaagatcggtcgcatcgacctggcccaagctgcacatc  
gaaatgccgtcaaccaagctctgataagttggtaagaccaaatacgccgagcatatcgcccgagccgctgcgacatc  
caagctccggatgcctccgctcgaaagtagcgctctgctgctccatacaagcccaacacggcctccagaagaagatgtg  
gcgacctcgatattgggaaatccccgaacatcgctcgctccagtcacatgacgctgttatcgggccattgtccgtcaggac  
atgttggagccggaatcccgctgacgagtgccggacttcgggcagtcctcgggccaaagcatcagcaatcgccgatg  
cctgcgcgacgacgactgacggtgtcgctccatcacagtttggcagtgatacacatggggaatcgcaatcgccgatg  
aaatcacgcccattgtatgaccgattccttgcgtccggtccgaaatggggccgaacccgctcgctgctaagatcgccgc  
agcatcgcatccatggcctccgcgacccggtcgagaacagcgggagttcggttccagggcaggtcttgcacgtgacac  
cctgtgcacgcccggagatgcaataggtcaggtctcgctaaatccccaaatgtcaagcacttccggaatcgggagcg  
gcgatgcaagtgccgataaaacataacgacttcttggtagaaacatcgggcagctatttaccgcaggacatccacg  
ccctccatcatcgaaagctgaaagcacgagattcttgcctccgagagctgcatcaggtcgagacgctgtcgaaactt  
cgatcagaaacttctcgacagacgtcggtgagttcaggttctttaaactcgactaaacacatgtaagcatgtgcaacgagcc  
cacgtcccggtgttgcggggcctagacgttcttgcgtcaggttcttgcgcgttcttgcaggtgtatcttatacacg  
ttccacaactatccaaactcacaaagtggaacttgcgtcaggttgcgtcaggttgcgtcaggttgcgtcaggttgc  
cgcgagggcactgtgcgcaggtgggggttccgctgcctgcaaaaggtgcgtcacaggttgcgttgcgttgcgttgc  
tccCAGAGGAACCTGCTTCTTACGACATTCACAGACCTTGCACTTCTTTGGCGAGAGGGGAAAGACCCctagactaga  
ccaagcttctggatttccattctgaagtttgaatttctgagtcactagtaattctccttggagatgtagtctgaatttcc  
tctgcaagagtacaaagattggcttcttggagatctttaaataatgtgtcactacgcttcttcttccatgaagttgat  
cgaatcagaagcagttgaacttctgctgttcttggagatgtgtcacttcttcttcttccatgaatcttcttcttccat  
tcaacatcagataaaatttatggcactgtttaaactgacttagtgtcatgactccagcaatagtggtgatataattactcaag  
cttctgcatgttcttctgacttcttcttcttccacaaacaaatagtggaattggcaaatggcaaatggcaaatggca  
ccaacgggttccggtcccttcaactgagccacggggccgacaatcttctggtcttctggggtgagatgtcccgttaggg  
tgacacaggtgagggagttcgacgactggcttggtagtagtagttcaacttctgaaggactggcagacagaaactgaa  
acttattatctgtgctccctcaatggcagaaacagtttcgacgaattcagcttcttcttccacgttatcttctgtggaat  
gaagccataagacaacgaaggtggctggggagtttggagctggagttctggaagggccaaagacatcttctgtggaat  
ggaccccaacactcacataccaggtccaccttctgacaaagttcggtccatcttcttggaaagattcggagttcgg  
gtgctgtggcttagcttctccactcccccaggaataatcgactcacccagcagcaggttctcagcagaaagcgggtc  
aacggtgagggccaatgGTGGCTTTTACCAACAGTACCCGGAATGCCAAGCTTGCGGCCCTTAAGAGCTGTAAATGAACTGG  
GAGTGGACACCTGTGGAGAGAAAGGCAAGGTGGATGTCAGTAAGACCAATAGGTGCCCTATCAGAAACGCAAGAGTCTTCT  
CTGTCTCGACAAGCCCAGTTTCTATTGGTCTCTCTTAAACCTGTCTTGTAACTTGATCTTACCTGCCAGTGCCCTCAG

27 / 28

FIG. 13C

ACCAACTTctgcaggaaattcctggacagctcccagatgatcagtaaccgtggtgttatttctgtgccgggcagtgagc  
ctgggtaggggagctctgctcagtgcttctcagctaaaaatgggtgggaaccccCaggggcccggccctggaa  
gtcccttctctctgttcttgggaagtcgattgagcaaacagcggggtcaggtgaggtccttcaataccgatgcaca  
ccgagtgctggggaggttctctctctcagggcccaacCccagggcccttgcctaggtcccggaactctCactcttgac  
gcatgcgtggcttgggtggtccagtcagcaaaacttgggttcccggttgcctgggaaggagggtaactgggcatcgacg  
cctctgtccacgaaagccttgtgaagaaaggttggggcgcttcttgtcagggagaaatgagggcgcaactggagtgaaactg  
gccccggggGcgctgtccccagatgtgtgtcagggcctctctgtatggcgcagccctgttccctgtgacccgcttggag  
ctggcacccctgagtggtggcctcaactTGTACTCACTCCAGGTCACTGTCTctcgacgcggccgctCGACgataAAATAA  
AAGATTtTATTAGTCTCCAGAAAAAGGGGGGAATGAAGAACCCCACTGTAGGTTTGGCAAgctagcTTAAGTAACCCA  
TTTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAgTTCAGATCAAGGTCGGAACAGATGGAACAGGCAATAAA  
AGAGCCCAACAACCCCTCACTCGGGGGCCAGTCCTCCGATTGACTGAGTCGCCCGGTACCCGTGTATCCAATAAACCCCT  
CTTGCAgTTGCATCCGACTTGTGGTCTCGCTGTTCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGG  
TCTTTTcaca tgcagCATGTATCAAAAATTAAATTGGTTTtTCTTAAGTATTACATTAAATGGCCATagtttccGTAAT  
CATGGTCATAGCTGTTTCCCTGTGTGAAATTGTTATCCGCTCACAAATTCACACAACATACGAGCCGGAAGCATAAAGTGT  
AAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACTACATTAATTGCGTTGGCTCACTGCCCCGCTTCCAGTCGGGAAACCT  
GTCGTGCCAGCTGCATTAA TGAAATCGGCCAACGCGGGGAGAGGGGTTTGCGTATTGGGGCGCTCTTCCGCTTCCCTCG  
TCACTGACTCGCTCGGTCGGTTCGGCTCGGCGAGCGGTATCAGCTCACTCAAGGGGGTAATACGGTTATCCACA  
GAATCAGGGGATACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAATAAAGGCCGCTTGCT  
GGCGTTTtTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAACCAGACAG  
GACTATAAAGATACCAGGCGTTTCCCCCTGGAAAGCTCCCCCTCGTGCGCTCTCTGTTCAGACCCCTGCCGCTTACCGGATAC  
CTGTCCGCCCTTCTCCCTTCGGGAAGCGTGGCGCTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGGTAGGTCGT  
TCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTACGCCCGACCGCTGCGCCTTATCCGGTAACATATCGTCTTGAGT  
CCAACCCGGTAAGACACGACTTATCGCCCACTGGCAGCAGCCCACTGGTAACAGGATTAGCAGACGAGGTATGTAGCGGGT

28 / 28

GCTACAGATTCTTGAAGTGGTGGCCCTAATACGGCTACACTAGAAAGGACAGTATTGGTATCTGCGCTCTGCTGAAGCC  
AGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAAACCAACCCGCTGGTAGCGGTGGTTTTTTGTTTGC  
AGCAGCAGATTACGCCGACAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAAAC  
GAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAG  
TTTGCGCAAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCT  
CAGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCCCGTGTGTAGATAACTACGATACGGGAGGGCTTACCA  
TCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTATATCAGCAATAAACCCAGCCAGCCGG  
AAGGGCCGAGCGCAGAAAGTGGTCTTGCAACTTTATCCGCCCTCCATCCAGTCTATTAATTGTTGCCGGAAGCTAGAGTAA  
GTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTGCCATTGCTACAGGCATCGTGGTGTACGCTCGTCTGTTGGTATG  
GCTTCATTCAGCTCCGGTTCCCAACGATCAAGCGAGTTACATGATCCCCCATGTTGTGCAAAAAGCGGTTAGCTCCTT  
CGGTCCCTCCGATCGTTGTCAAGAAAGTAAAGTTGGCCGAGTGTATCACTCATGTTATGGCAGCAGTGCATAATTCTCTTA  
CTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtaactcaaccaagtcattctgagaaatagtgatgcgagcga  
ccgagttgctcttgcggcggtcaacacgggataaataccggccacacatagcagaactcttaaaagtgtctcatcttgga  
acgttcttcggggcgaaaactctcaaggatcttacggctgttgagatccagttcgatgtaccactcgtgcacccaa  
gatcttcagcatctttactcttcacagcggttctggtgagcaaaaaacgggaaggcaaaatgcgcgaagggaata  
agggcgacacgggaaatgttgataactcatactctctctcttccaatatatttgaagcatttatcagggttattgtctcat  
gacattaacctataaaaaataggcgt

FIG.\_ 13D